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OVERNIGHT COURIER 11/11/02

Dockets Management Branch
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Citizen Petition

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food Drug and Cosmetic Act and in accordance with 21 CFR 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to declare that the drug products, Methadone Hydrochloride Tablets, USP, 15 mg, 20 mg and 30 mg are suitable for consideration in abbreviated new drug applications (ANDAs).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration declare that Methadone Hydrochloride Tablets, USP, 15 mg, 20 mg, and 30 mg are suitable for submission as ANDAs. The listed reference drug product upon which this petition is based is Methadone Hydrochloride Tablets USP, 40 mg approved under NDA 17-058 (see Attachment 1). The petitioner thus seeks a change in strength (from a 40 mg tablet to include tablet strengths of 15 mg, 20 mg, and 30 mg) from that of the listed drug product.

B. Statement of Grounds

The reference listed drug (RLD) product is currently available in a tablet containing 40 mg of Methadone Hydrochloride. The proposed drug products also represent tablets that will contain the following additional strengths of the drug: 15 mg, 20 mg, and 30 mg. The newly proposed strengths (15 mg, 20 mg and 30 mg) are believed to be consistent with the currently approved RLD product's labeling and will provide a more convenient single solid oral dosage unit to provide the specific dose prescribed by the physician for the individual patient. The petition is thus seeking a change in strength (from 40 mg to include additional tablet strengths of 15 mg, 20 mg and 30 mg) from that of the reference listed drug product.

The approved labeling of the RLD lists two indications for methadone hydrochloride tablets, detoxification treatment and maintenance treatment of narcotic addiction. The dosage and administration section of the labeling reads as follows for the detoxification indication:

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"For detoxification treatment – The drug shall be administered daily under close supervision as follows:

A detoxification treatment course shall not exceed 21 days and may not be repeated earlier than four weeks after completion of the preceding course.

In detoxification, the patient may receive Methadone when there are significant symptoms of withdrawal. The dosage schedules indicated below are recommended, but could be varied in accordance with clinical judgment. Initially, a single oral dose of **15 mg to 20 mg** of Methadone will often be sufficient to suppress withdrawal symptoms. **Additional** Methadone may be provided if withdrawal symptoms are not suppressed or if symptoms reappear. When patients are physically dependent on high doses, it may be necessary to exceed these levels. **40 mg / day** in single or divided doses will usually constitute an adequate stabilizing dosage level. Stabilization can be continued for 2 - 3 days, and then the amount of Methadone normally will be gradually decreased." (Emphasis added).

There are general guidelines for initiation of therapy with Methadone Hydrochloride for narcotic maintenance (i.e., the initial dose should be sufficient to "control the abstinence symptoms that follow withdrawal of narcotic drugs but should not be so great as to cause sedation, respiratory depression or other signs of intoxication. If a patient has been a heavy user of Heroin up to the day of admission, he / she may be given 20 mg 4 to 8 hours later or 40 mg in a single oral dose". The labeling indicates that doses are to be individualized according to the response of the patient and usually shall not exceed 120 mg / day. Doses above that level must be justified in the patient's medical record.

It is clear from the labeling of the approved drug product that dosage strengths of 15 mg, 20 mg, 30 mg and 40 mg are clearly contemplated for the approved indications. For detoxification treatment doses of 15 mg, 20 mg and up to (which includes a 30 mg dose) 40 mg as a single dose are appropriate. For maintenance treatment, initial doses are individualized to the patient's response and may be adjusted on a total daily dosage basis of usually up to 120 mg. The availability of various dosage strengths will provide the treating physician and facility with options to select the appropriate strength tablets, or combination of tablet doses to fulfill individual patient needs, while eliminating the need to break larger size tablets to obtain the appropriate dose.

The petitioner is seeking the requested changes in strength from the RLD drug product to provide the physician greater flexibility in administering alternate dosage strengths that are consistent with doses contemplated in the approved labeling of the RLD. The goal being to reduce the number of tablets a patient would need to take for a single dose. This will improve patient convenience, compliance and make it easier to achieve the required dose for those patients that either have difficulty in swallowing multiple tablets or because of their illness make multiple tablet administration more difficult.

Copies of labeling of the reference listed drug product upon which this petition is based and draft labeling for the proposed product are included in Attachments 2 and 3, respectively. The proposed labeling is the "same as" the approved RLD labeling with the exception of changes allowed because the manufacturer of the generic product differs from that of the RLD and in the How Supplied section, which lists the additional available strengths sought by this petition.

There are no changes in the indications, conditions of use or dosage and administration sections necessary as the approved labeling of the RLD already contemplates the use of the proposed dosage strengths.

Therefore, the petitioner requests that the Commissioner find that a change in strength from a 40 mg tablet to include 15 mg, 20 mg and 30 mg strength tablets for this proposed product raises no questions of safety or effectiveness, and the Agency should then approve the petition.

Because this petition requests only a change in strength to include tablets of 15 mg, 20 mg and 30 mg from that of the reference listed drug product, it is not the type of petition that would have been covered by the provisions of the pediatric final rule. In addition, because of the October 17, 2002 ruling of Judge Henry H. Kennedy, Jr. in the matter of Association of American Physicians and Surgeons, Inc. v United States Food and Drug Administration, Civil Action No. 02-02898, finding that the FDA's "Pediatric Final Rule" was arbitrary and capricious, there is no apparent reason to address the provisions of that rule in consideration of this petition.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

D. Economic Impact

The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis, if requested by the Agency.

E. Certification

The undersigned certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

Robert Pollock

Robert W. Pollock
Vice President

RWP/pk

Attachments

cc: G. Davis (OGD), M. Shimer (OGD), L. Lachman

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